Temporal pattern processing is behaviorally and intergenerationally modulated by the tyraminergic/octopaminergic system in *C. elegans*.

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C. elegans Neuronal Development, Synaptic Function & Behavior, July 2022
University of Vienna, Austria

The ability of an animal to recognize patterns in the timing of stimuli in its environment, associate the relevant events, and respond appropriately when subsequent events reoccur is key to survival. How molecular and cellular factors interact to define relevant timescales and react in proper sensory “time windows” is a fundamental problem. I have designed a novel trial-by-trial associative learning paradigm that allows responses to timing patterns to be investigated using *C. elegans*. *C. elegans* can associate a neutral odor stimulus with a noxious light stimulus when they are paired in time, and worms respond differentially when the ordering of these two stimuli is varied. Different temporal structures of exposures can be generated by introducing timing gaps between the odor and the light. Conditioning that occurs when the neutral odor is presented some time after the light is known as trace-conditioning, as opposed to standard Pavlovian conditioning that occurs when there is no temporal gap. Worms can perform trace-conditioning and are decreasingly sensitive to increased trace periods. Human trace-conditioning is thought to be associated with “awareness,” as opposed to standard-conditioning, which does not require the subject to be aware of the predictive relationships between stimuli. From a candidate screen of biogenic amine neuromodulators, I found that dopamine, serotonin and tyramine/octopamine are all involved in controlling the standard- conditioning response. However, only the tyraminergic/octopaminergic system modulates trace-conditioning. Adapting to the environment is crucial not only for the survival of an individual but also critical for its future progeny. Worms exposed to learning in the parental generation produced progeny with altered trace responses. The order and timing of the stimuli pattern encountered dictated this intergenerational adaptation: only worms exposed to ordered odor-light stimuli modulated intergenerational timing adaptation. Worms experiencing identical levels of odor-light stimuli but in a randomly shuffled pattern showed no intergenerational adaptation. Intriguingly, tyramine seems to be involved in this intergenerational inheritance. Determining the mechanisms that enable a purely cognitive element such as patterned timing recognition to affect intergenerational modulation of responses to timing patterns might uncover new biology that informs us about how parental experiences can impact future generations.